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(57) Abstract

A freeze-resistant topical germicide for application to skin, such as the teat of a dairy cow. The germicide may be a one-part composition or a two-part system. The one-part disinfecting composition comprises an organic acid germicide and a non-esterifying antifreeze. The two-part system comprises a first part and a second part adapted to be mixed to yield the disinfecting composition. The first part comprises a metal chlorite and a chlorite-stable antifreeze, and the second part comprises an organic acid germicide and a non-esterifying antifreeze, or an inorganic acid and either an alcohol or a non-esterifying antifreeze.

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FREEZE-RESISTANT TOPICAL GERMICIDES AND METHODS RELATED THERETO

TECHNICAL FIELD

The present invention is generally directed to freeze-resistant topical germicides for application to skin, particularly the teat of a dairy cow, wherein the germicide is a one-part disinfecting composition containing an organic acid germicide and an non-esterifying antifreeze, or a two-part system comprising a first part and a second part adapted to be mixed to yield a disinfecting composition.

BACKGROUND OF THE INVENTION

A constant winter problem on many dairies across the country is chapping teats, the problem being more severe in the Northern tier of the United States and Canada. As temperatures drop, teats become more chapped and cracked. This generally results in the elevation of the somatic cell counts of the affected cows, and often delays the milking process because cows refuse to let down milk when their teats are irritated. Furthermore, research studies have repeatedly shown that *Staphylococcus aureus* infections of the milk go up dramatically on damaged teats, leading to an increase in the number of quarters that are infected with this organism. Another problem is that of logistics, where pre- and post-milking teat dips that are susceptible to freezing cannot be stored in milking facilities which are exposed to sub-freezing ambient temperatures.

Even when the dips are maintained in a non-frozen state, cows that have been post-dipped must stay protected from freezing temperatures until the teat dip dries. This approach is practicable in stanchion barns, but not in milking parlors. Thus, to prevent the teat dip from freezing on the teat, some dairymen allow the dip to remain on the teat for about 45 seconds after dipping, and then blot off the excess dip before the cows go outdoors. Such additional measures, however, are time-consuming and not always effective.

For these reasons, dairymen are advised to stop post-milking dipping during weather conditions where freezing and chapping are likely to occur. Since bacterial transfer and proliferation tend to be lower in colder environments, dairymen must balance the potential problems associated with freezing and chapping with the potential for elevated somatic cell counts and clinical mastitis, often choosing to forgo the use of post-milking dips in freezing weather conditions. Other dairymen elect to switch to dips with higher levels of skin softeners and emollients as the temperatures drop, while still others elect dry powder dips, which are basically moisture absorbers with little antimicrobial effectiveness.

In an attempt to avoid the above problems, freeze-resistant teat dips have been proposed. For example, a teat-dip composition which freezes below -20°C is disclosed in Japanese Patent No. 8175989. The base composition of the dip, as provided in one example of that document, comprises about 30% each of propylene glycol and lactic acid, and 7% sorbitan. Further, a freeze-resistant teat dip, containing chlorhexidine disinfectant, and at least 80 wt% of a volatile alcohol, is disclosed in U.S. Patent No. 4,434,181.

More recently in the United States, a non-freezing teat dip has been commercialized which contains, as its base, over 60 wt% of propylene glycol. The active germicide in the product is a combination of C8 and C10 alkanoic acids. The shelf-life of this product is limited, however, due to tendency of the acid to react with the glycol to form esters, which continuously reduces the amount of available acid in the formulation and thus the product's effectiveness. For example, periodic analysis of such a teat dip indicates a loss of 20% of the acid in only a six-month period at ambient conditions, and over a 10% loss of the acid in just one-month at 100°F. A similar problem is encountered if one were to introduce glycol-types of antifreeze into other acid-containing germicidal teat dips. This includes those dips where the acid is present as a buffering agent, such as in iodophor dips where citric acid is used to maintain a pH range at which the iodine species are optimally effective (*e.g.*, pH 4-5).

Accordingly there is a need in the art for improved teat dip compositions which resist freezing in ambient winter conditions, resist reacting with acidic

germicides and/or acid buffering agents, and maintain compatibility of the freeze-resistant agent with the antimicrobial agent. The present invention fulfills these needs and provides further related advantages.

SUMMARY OF THE INVENTION

In brief, the present invention is directed to freeze-resistant topical germicides for application to, for example, the teat of a dairy cow. Such compositions resist freezing in ambient winter conditions, and do not react with organic acidic germicides and/or buffering agents. Further, the compositions of this invention maintain compatibility between the freeze-resistant and antimicrobial agents.

The topical germicides of this invention may generally be classified as one-part or two-part formulations. The one-part formulation comprises an organic acid germicide and an non-esterifying antifreeze, while the two-part formulation (hereinafter referred to as a "system") comprises a first part and a second part adapted to be mixed to yield the topical germicide. In the two-part system, the first part comprises a metal chlorite and a chlorite-stable antifreeze, while the second part comprises (a) an organic acid germicide and a non-esterifying antifreeze, or (b) an inorganic acid and either an alcohol or a non-esterifying antifreeze.

Accordingly, in one embodiment of this invention, a one-part freeze-resistant aqueous disinfecting composition is disclosed containing an organic acid germicide and an non-esterifying antifreeze, wherein the non-esterifying antifreeze contains from 4 to 16 carbon atoms and has no primary carbon atom bearing a hydroxyl group. Non-esterifying antifreezes my be an ether having at least one ether linkage between two carbon atoms, an ether-alcohol having at least one ether linkage between two carbon atoms and with at least one secondary carbon atom bearing a hydroxyl group, or an ester having at least one ester linkage between two carbon atoms.

In one aspect of this embodiment, the non-esterifying antifreeze has the structure R^1-O-CH_2-CH(OR^2)-R^3, wherein R^1 is C_{1-8}alkyl, and R^2 and R^3 are the same or different and independently selected from hydrogen or C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group.

Representative antifreezes include those compounds wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen, and R^3 is C_{1-8}alkyl moiety; wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen and R^3 is methyl; and wherein R^1, R^2 and R^3 are C_{1-8}alkyl.

In another aspect of this embodiment, the non-esterifying antifreeze has the structure R^4-CH(OR^5)-CH_2-O-CH_2-CH(OR^2)-R^3, wherein R^2, R^3, R^4 and R^5 are the same or different and independently selected from hydrogen and C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group. Representative antifreezes include those compounds wherein R^4 is C_{1-8}alkyl and R^5 is hydrogen; and wherein R^4 is C_{1-8}alkyl and R^5 is C_{1-8}alkyl.

Non-esterifying antifreezes also include compounds of the above structures wherein at least one oxygen atom is bound to -CO(C_{1-8}alkyl) to form an ester.

Typical non-esterifying antifreezes of this invention include propylene glycol monomethyl ether having the structure $CH_3OCH_2CH(OH)CH_3$, propylene glycol monoethyl ether having the structure $CH_3CH_2OCH_2CH(OH)CH_3$, propylene glycol monopropyl ether having the structure $CH_3CH_2CH_2OCH_2CH(OH)CH_3$, propylene glycol monoisopropyl ether having the structure $CH_3CH(CH_3)OCH_2CH(OH)CH_3$, dipropylene glycol having the structure $CH_3CH(OH)CH_2OCH_2CH(OH)CH_3$, dipropylene glycol methyl ether having the structure $CH_3CH(OCH_3)CH_2OCH_2CH(OH)CH_3$, dipropylene glycol ethyl ether having the structure $CH_3CH(OCH_2CH_3)CH_2OCH_2CH(OH)CH_3$, and dipropylene glycol acetate having the structure $CH_3CH(OCOCH_3)CH_2OCH_2CH(OH)CH_3$.

The non-esterifying antifreeze may be present at a concentration ranging from about 10% to about 75% by weight of the composition, and typically from 15% to 50% by weight of the composition.

The organic acid germicide may be an alpha-hydroxy carboxylic acid having a pKa between about 2.8 and about 4.2, such as glycolic acid, lactic acid, malic acid, mandelic acid, citric acid, tartaric acid, and mixtures thereof. Other organic acid germicides include formic acid, acetic acid, propionic acid, benzoic acid, caprylic acid, capric acid, hydroxybenzoic acid, and mixtures thereof.

The organic acid germicide is present at a concentration between about 0.25% and about 7.5% by weight of the disinfecting composition, and typically from 2% and 5% by weight of the disinfecting composition.

The disinfecting composition may be formulated as solution, cream or gel, and may include one or more optional components such as a textural modifier, a surfactant, an odorant, a colorant, and mixtures thereof.

In another embodiment of this invention, a two-part freeze-resistant disinfecting system is disclosed comprising a first part and a second part adapted to be mixed to yield an aqueous disinfecting composition. The first part, prior to mixing, comprises a metal chlorite and a chlorite-stable antifreeze. The second part, prior to mixing, comprises (a) an organic acid germicide and a non-esterifying antifreeze, or (b) an inorganic acid and either an alcohol or a non-esterifying antifreeze. The chlorite-stable and non-esterifying antifreezes contain from 4 to 16 carbon atoms and have no primary carbon atom bearing a hydroxyl group.

The metal chlorite of the first part is an alkali or alkaline earth chlorite, such as sodium chlorite or potassium chlorite, and is typically sodium chlorite. The metal chlorite is present in the first part at a concentration such that, when combined with the second part, it is present within the disinfecting composition at a concentration ranging from about 0.005% to about 1% by weight, generally from 0.05% to 0.5% by weight, and typically from 0.1% to 0.4% by weight.

The chlorite-stable antifreeze is as disclosed above with regard to the non-esterifying antifreeze of the freeze-resistant aqueous disinfecting composition. The chlorite-stable antifreeze is present within the first part at a concentration ranging from about 10% to about 75% by weight, and typically from 15% to 50% by weight of the first part.

In one aspect of the two-part system, the second part comprises an organic acid and a non-esterifying antifreeze. The organic acid and the non-esterifying antifreeze of the second part is as disclosed above with regard to the organic acid and the non-esterifying acid of the freeze-resistant aqueous disinfecting composition. In

other words, the one-part disinfecting composition may be employed as the second part of the two-part system.

In another aspect of the two-part system, the second part comprises an inorganic acid and either an alcohol or a non-esterifying antifreeze. Representative inorganic acids include phosphoric acid, monosodium acid phosphate, sulfuric acid, hydrochloric acid, or sodium bisulfate. The inorganic acid is present in the second part at a concentration such that, when combined with the first part and before reacting therewith, it is present within the disinfecting composition at an initial concentration ranging from 0.001% to 2% by weight, and typically from 0.01% to 1.0% by weight.

Representative alcohols include polyols, such as glycerine, sorbitol and propylene glycol, while the non-esterifying antifreeze is as disclosed above with regard to the non-esterifying antifreeze of the freeze-resistant aqueous disinfecting composition. The alcohol or the non-esterifying antifreeze is present within the second part at a concentration ranging from about 10% to about 75% by weight, and typically from 15% to 50% by weight of the second part.

The first and second parts of the two-part freeze resistant system of this invention may be independently formulated as solutions, creams or gels, and may further include one or more optional components such as a textural modifier, a surfactant, an odorant, a colorant, and mixtures thereof.

In yet a further embodiment, methods are disclosed for disinfecting a substrate by contacting the substrate with an effective amount of the one-part freeze-resistant aqueous disinfecting composition of this invention, or the disinfectant composition resulting from the combination of the first and second parts of the two-part freeze-resistant disinfecting system of this invention. Suitable substrates in this regard include skin and, more specifically, the teat of a dairy cow.

These and other aspects of the present invention will be evident upon reference to the following detailed description.

DETAILED DESCRIPTION OF THE INVENTION

Freeze resistance has traditionally been imparted to aqueous systems, such as radiator coolants, by incorporation therein of such water-soluble alcohols as methanol (a mono-hydroxy compound) or glycols (which contain two alcoholic functions) such as ethylene glycol. Molecules which contain a greater number of hydroxyl groups (referred to as "polyols"), such as glycerin and sugars, are also known to depress aqueous freezing points. In all cases, the greater the concentration of alcoholic solute, the lower the freezing point, with the degree of depression depending on the solute. For example, to attain a freezing point of 0°F requires an aqueous concentration of methanol of about 28% by weight, about 43% by weight for glycerin and about 34% by weight for ethylene glycol.

In order to create a freeze-resistant teat dip formulation, particularly one which incorporates organic acids as either active ingredients or buffers, the above alcohols are not suitable. This is due to esterification of the hydroxyl moiety by reaction with the carboxylic acid of the organic acid. For example, the use of a material such as propylene glycol to reduce the freezing temperature of a teat dip, in which organic acids are either the germicide or the source of buffering, is counterindicated by the tendency for the acid to esterify and lose germicidal functionality. Furthermore, in such compositions the lower levels of acid which result give rise to higher pH formulations, so that the remaining acid will tend to exist to a greater degree in the non-functioning anionic form.

It has been found that esterification of secondary hydroxyl groups, such as the hydroxyl at the 2-position of propylene glycol, is less favored due to both electronic and steric factors. However, esterification of primary alcohols, such as the hydroxyl at the 1-position of propylene-glycol, proceeds at an unacceptably fast rate. Thus, in the practice of this invention, a non-esterifying antifreeze is employed in combination with one or more organic acids. Such non-esterifying antifreeze agents generally contain from 4 to 16 carbon atoms, and contain one or more ether, secondary alcohol and/or ester moieties. Such non-esterifying antifreezes do not, however, contain any primary carbon bearing a hydoxyl group.

Accordingly, in one embodiment of this invention, a freeze-resistant aqueous disinfecting composition is disclosed containing an organic acid germicide and an non-esterifying antifreeze, wherein the non-esterifying antifreeze contains from 4 to 16 carbon atoms and has no primary carbon atom bearing a hydroxyl group. Suitable non-esterifying antifreezes may be generally characterized as an ether having at least one ether linkage between two carbon atoms, an ether-alcohol having at least one ether linkage between two carbon atoms and with at least one secondary carbon atom bearing a hydroxyl group, or an ester having at least one ester linkage between two carbon atoms.

Representative non-esterifying antifreezes have the structure R^1-O-CH_2-$CH(OR^2)$-R^3, wherein R^1 is C_{1-8}alkyl, and R^2 and R^3 are the same or different and independently selected from hydrogen or C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group. Suitable compounds are those wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen and R^3 is C_{1-8}alkyl moiety; wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen and R^3 is methyl; and wherein R^1, R^2 and R^3 are C_{1-8}alkyl. In another embodiment, representative non-esterifying antifreezes have the structure R^4-$CH(OR^5)$-CH_2-O-CH_2-$CH(OR^2)$-R^3, wherein R^2, R^3, R^4 and R^5 are the same or different and independently selected from hydrogen and C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group. Suitable compounds are those wherein R^4 is C_{1-8}alkyl and R^5 is hydrogen; and wherein R^4 is C_{1-8}alkyl and R^5 is C_{1-8}alkyl. Non-esterifying antifreezes also include compounds of the above structures wherein at least one oxygen atom is bound to -$CO(C_{1-8}$alkyl) to form an ester.

More specific representative non-esterifying antifreezes of this invention include (but are not limited to) propylene glycol monomethyl ether (CH_3-$OCH_2CH(OH)CH_3$) propylene glycol monoethyl ether (CH_3CH_2-$OCH_2CH(OH)CH_3$), propylene glycol monopropyl ether ($CH_3CH_2CH_2$-$OCH_2CH(OH)CH_3$), propylene glycol monoisopropyl ether ($CH_3CH(CH_3)$-$OCH_2CH(OH)CH_3$), dipropylene glycol ($CH_3CH(OH)CH_2OCH_2CH(OH)CH_3$), dipropylene glycol methyl ether ($CH_3CH(OCH_3)CH_2OCH_2CH(OH)CH_3$), dipropylene glycol ethyl ether

($CH_3CH(OCH_2CH_3)CH_2OCH_2CH(OH)CH_3$), and dipropylene glycol acetate ($CH_3CH(OCOCH_3)CH_2OCH_2CH(OH)CH_3$).

Preferred non-esterifying antifreezes are those that are soluble in water at ambient winter temperatures to at least 1 part by weight of compound per 4 parts of water. Their concentration should be from about 10% to about 75% by weight, and typically from 15% to 50% by weight of the disinfecting composition. The freezing point of the disinfecting composition should be at or below 14°F (-10°C), generally below about 7°F (-14°C), and typically below about 0°F (-18°C).

The organic acid germicide may be an alpha-hydroxy carboxylic acid having a pKa between about 2.8 and about 4.2, such as glycolic acid, lactic acid, malic acid, mandelic acid, citric acid, tartaric acid, and mixtures thereof. Other organic acid germicides include formic acid, acetic acid, propionic acid, benzoic acid, caprylic acid, capric acid, hydroxybenzoic acid, and mixtures thereof. The organic acid germicide is present at a concentration between about 0.25% and about 7.5% by weight of the disinfecting composition, and typically from 2% and 5% by weight of the disinfecting composition.

The pH of the mixed disinfecting composition should lie in the range of about 2 to about 5, and typically from about 2.4 to about 4.5. When organic acids, such as citric, are employed primarily as buffering agents, rather than for germicidal activity, such as for pH adjustment or iodophor formulations, their level of use is generally in the range of about 0.1% to about 1.0%, where the amount utilized depends to a significant degree on the chemical characteristics of the specific formulation.

In another embodiment of this invention, a two-part freeze-resistant disinfecting system is disclosed comprising a first part and a second part adapted to be mixed to yield an aqueous disinfecting composition. The first part, prior to mixing, comprises a metal chlorite and a chlorite-stable antifreeze. The second part, prior to mixing, comprises (a) an organic acid germicide and a non-esterifying antifreeze, or (b) an inorganic acid and either an alcohol or a non-esterifying antifreeze. The chlorite-stable and non-esterifying antifreezes contain from 4 to 16 carbon atoms and have no primary carbon atom bearing a hydroxyl group.

In the two-part system, the metal chlorite of the first part is an alkali or alkaline earth chlorite, such as sodium chlorite or potassium chlorite, and is typically sodium chlorite. The metal chlorite is present in the first part at a concentration such that, when combined with the second part, it is present within the disinfecting composition at a concentration ranging from about 0.005% to about 1% by weight, generally from 0.05% to 0.5% by weight, and typically from 0.1% to 0.4% by weight of the disinfecting composition.

The chlorite-stable and non-esterifying antifreezes of the first and second parts, respectively, may be the same or different. Such antifreezes contain from 4 to 16 carbon atoms and have no primary carbon atom bearing a hydroxyl group. In the case of the chlorite-stable antifreeze, a primary alcohol will oxidize upon contact with chlorite, and is thus to be avoided. The chlorite-stable and non-esterifying antifreezes may be an ether having at least one ether linkage between two carbon atoms, an ether-alcohol having at least one ether linkage between two carbon atoms and with at least one secondary carbon atom bearing a hydroxyl group, or an ester having at least one ester linkage between two carbon atoms.

Representative chlorite-stable and non-esterifying antifreezes have the structure R^1-O-CH_2-CH(OR^2)-R^3, wherein R^1 is C_{1-8}alkyl, and R^2 and R^3 are the same or different and independently selected from hydrogen or C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group. Suitable compounds are those wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen and R^3 is C_{1-8}alkyl moiety; wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen and R^3 is methyl; and wherein R^1, R^2 and R^3 are C_{1-8}alkyl. In another embodiment, representative chlorite-stable and non-esterifying antifreezes have the structure R^4-CH(OR^5)-CH_2-O-CH_2-CH(OR^2)-R^3, wherein R^2, R^3, R^4 and R^5 are the same or different and independently selected from hydrogen and C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group. Suitable compounds are those wherein R^4 is C_{1-8}alkyl and R^5 is hydrogen; and wherein R^4 is C_{1-8}alkyl and R^5 is C_{1-8}alkyl. Chlorite-stable and non-esterifying antifreezes also include compounds of the

above structures wherein at least one oxygen atom is bound to -CO(C_{1-8}alkyl) to form an ester.

More specific representative chlorite-stable and non-esterifying antifreezes of this invention include (but are not limited to) propylene glycol monomethyl ether (CH_3-$OCH_2CH(OH)CH_3$) propylene glycol monoethyl ether (CH_3CH_2-$OCH_2CH(OH)CH_3$), propylene glycol monopropyl ether ($CH_3CH_2CH_2$-$OCH_2CH(OH)CH_3$), propylene glycol monoisopropyl ether ($CH_3CH(CH_3)$-$OCH_2CH(OH)CH_3$), dipropylene glycol ($CH_3CH(OH)CH_2OCH_2CH(OH)CH_3$), dipropylene glycol methyl ether ($CH_3CH(OCH_3)CH_2OCH_2CH(OH)CH_3$), dipropylene glycol ethyl ether ($CH_3CH(OCH_2CH_3)CH_2OCH_2CH(OH)CH_3$), and dipropylene glycol acetate ($CH_3CH(OCOCH_3)CH_2OCH_2CH(OH)CH_3$).

Preferred chlorite-stable and non-esterifying antifreezes are those that are soluble in water at ambient winter temperatures to at least 1 part by weight of compound per 4 parts of water. Their concentration should be from about 10% to about 75% by weight, and typically from 15% to 50% by weight of the disinfecting composition. The freezing point of the disinfecting composition should be at or below 14°F (-10°C), generally below about 7°F (-14°C), and typically below about 0°F (-18°C).

In one embodiment of the two-part system of this invention, the second part comprises an organic acid and a non-esterifying antifreeze. In this aspect, the second part may be the freeze-resistant aqueous disinfecting composition as disclosed above, containing an organic acid and a non-esterifying antifreeze. Thus, the organic acid germicide may be an alpha-hydroxy carboxylic acid having a pKa between about 2.8 and about 4.2, such as glycolic acid, lactic acid, malic acid, mandelic acid, citric acid, tartaric acid, and mixtures thereof. Other organic acid germicides include formic acid, acetic acid, propionic acid, benzoic acid, caprylic acid, capric acid, hydroxybenzoic acid, and mixtures thereof. The organic acid germicide is present in the second part such that, following mixture with the first part, it has a concentration between about 0.25% and about 7.5% by weight of the disinfecting composition, and typically from 2% and 5% by weight of the disinfecting composition. The non-

esterifying antifreeze of the second part in this embodiment is as disclosed above, and is present at a concentration such that, following mixture with the first part, it is present at a concentration from about 10% to about 75% by weight, and typically from 15% to 50% of the disinfecting composition.

In another embodiment of the two-part system, the second part comprises an inorganic acid in combination with either an alcohol or a non-esterifying antifreeze. The non-esterifying antifreeze of this embodiment is as disclosed above, while representative alcohols include polyols, such as glycerine, sorbitol and propylene glycol. Representative inorganic acids include phosphoric acid, monosodium acid phosphate, sulfuric acid, hydrochloric acid, sodium bisulfate, and mixtures thereof. The inorganic acid is present in the second part at a concentration such that, when combined with the first part and before reacting therewith, it is present within the disinfecting composition at an initial concentration ranging from 0.001% to 2% by weight, and typically from 0.01% to 1.0% by weight. The alcohol or non-esterifying antifreeze is present within the second part at a concentration such that, when combined with the first part, it is present in the disinfecting composition at a concentration from about 10% to about 75% by weight of the disinfecting composition, and typically from 15% to 50% by weight of the disinfecting composition.

Various optional ingredients may be included in the one-part freeze resistant aqueous disinfecting composition, as well as the first part, second part, or both first and second parts of the two-part system. Such ingredients include (but are not limited to) wetting agents, textural modifiers, film-forming polymers, colorants and mixtures thereof. The wetting agents facilitate contact of the disinfecting composition with the skin, and can be selected from those materials recognized to provide this effect, in both identity and amount. Textural modifiers are those materials which primarily affect the body of the mixed disinfecting composition in terms of retention, flow and lubricity. These include thickening agents such as alkyl celluloses, alkoxy celluloses, xanthan gum, guar gum, and polyacrylamide derivatives, of which the polymer of 2-acrylamido-2-methylpropane sulfonic acid is a preferred example. Other textural modifiers include lanolin derivatives, acyl lactylates, polyethylene glycol, glyceryl

esters, and mixtures thereof. Film-forming polymers include the above-referenced polyacrylamides, as well as the class of poly(vinyl alcohols/vinyl acetates) and polyvinyl pyrollidone. Colorants are generally selected from the group found acceptable for use in skin-contacting formulations, and are known to those skilled in the art.

In a further embodiment, a method for disinfecting a substrate is disclosed, wherein the method comprises contacting the substrate with an effective amount of the one-part freeze-resistant disinfecting composition of this invention, or contacting the substrate with an effective amount of the disinfecting composition formed by mixing the two-part disinfecting system of this invention. Suitable substrates include the skin or tissue of a warm-blooded animal and, in a preferred embodiment, the teat of a dairy cow.

In a further aspect of this invention, this invention is directed to a method for making a disinfecting composition comprising mixing the first part and the second part of the two-part disinfecting system, as well as mixing the respective compounds to form the first and second parts of the two-part system, and to form the one-part disinfectant composition. In one embodiment of the two-part system, both the first and second parts are aqueous solutions, creams or gels. In another embodiment, at least one of the first or second parts is in a concentrated form, and the concentrated form (either solid or liquid) is mixed with the other part and then diluted with water, or diluted with water and then mixed with the other part.

The following examples are by way of illustration only, and nothing therein should be taken as a limitation upon the overall scope of the invention.

EXAMPLE 1

This Example illustrates the preparation of a freeze-resistant germicidal formulation that remains free-flowing to below about 10°F (-12°C). It suppresses the chapping and cracking of skin to which it is applied, which might otherwise occur in sub-freezing temperatures.

Stir 0.50 gms of Natrosol 250MBR thickener into 25 gms of propylene glycol monomethyl ether, and then add 0.5 gms of Triton X-100 and 0.25 gms of Pluronic L-31 surfactants. Thereafter, dissolve the following three acid germicides into the mixture: 2 gms of mandelic acid, 0.2 gms of benzoic acid and 2 gms of propionic acid. Finally, dissolve 0.1 gms of citral odorant into the glycol ether mix. While stirring, add 0.05 mgs of FD&C Yellow #5 and 0.00005 gms of FD&C Yellow #33, followed by a quantity of water necessary to bring the weight of the mixture to 100 gms. Continue stirring until the thickener is fully dissolved. The viscosity of this formula is about 575 centipoise, when measured with a Brookfield RVF viscometer, using Spindle #3 at 20 rpm.

The gold-colored formulation, which has a citrus odor, can kill approximately 10^4 logarithms of the microbial pathogen *Staphylococcus aureus* deposited onto a simulated cow teat after 1 minute of contact. The residual germicide on the teat surface can also destroy at least 10^2 logarithms of the environmental pathogen *Streptococcus uberis* 12 hours after deposition onto the teat following a 30 minute contact.

EXAMPLE 2

The above Example 1 is repeated, using 35 gms of propylene glycol monomethyl ether, 0.1 gms of methyl salicylate in place of the citral, and 0.00065 gms of methylene blue in place of the yellow and red colorants. The blue formulation thus prepared has a wintergreen odor, remains liquid to below about 0°F (-18°C), and has a viscosity of 305 cps.

EXAMPLE 3

This example illustrates the use of the present invention in a two part chlorous acid-forming germicidal barrier teat dip, in which both parts, as well as the mixed formulation, remain fluid to a temperature below 0°F.

A first thickened liquid is prepared by mixing the following ingredients:

Coamedia brand poly (sulfonic acid), 16% solid	16.00%

Sodium hydroxide, 1N	16.00%
Sodium dodecylbenzene sulfonate	1.80%
Sodium chlorite	0.50%
Dipropylene glycol	32.00%
Hi-Sil T-600 (Silica)	2.50%
Water	q.s.

A second thickened liquid is prepared by mixing the following ingredients:

Malic acid	4.2%
Natrosol 250 MBR	1.00%
Dipropylene glycol monomethyl ether	35.00%
Sodium benzoate	0.04%
Poloxamer 188	0.40%
FD&C Yellow #5	0.20%
Water	q.s.

The two thickened liquids are blended, preferably within two hours before application. The resulting liquid remains fluid on the cow's teats throughout the intermilking period, preventing chapping and cracking, while providing continuous antimicrobial activity to suppress mastitis formation.

EXAMPLE 4

This example illustrates the use of the present invention in a freeze-resistant topical germicide which contains a film-forming agent and which remains fluid to below 0°F.

Disperse 2 gms of poly(vinyl alcohol), PVA-2408 into 65 gms of dipropylene glycol monomethyl ether, followed by the addition of 1 gms each of the germicidal agents caprylic acid, malic acid and glyceryl monolaurate. After the latter are dissolved, add 0.075 gms of methyl salicylate, stir and add 0.0001 gms of FD&C Blue #1 and 0.05 gms of FD&C Yellow #5 followed by sufficient water to take the

weight of the mixture to 100 gms. Continue stirring until the PVA is fully dissolved and the mixture becomes uniform.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

I claim:

1. A freeze-resistant aqueous disinfecting composition comprising an organic acid germicide and a non-esterifying antifreeze, wherein the non-esterifying antifreeze contains from 4 to 16 carbon atoms and has no primary carbon atom bearing a hydroxyl group.

2. The composition of claim 1 wherein the non esterifying antifreeze is an ether having at least one ether linkage between two carbon atoms.

3. The composition of claim 1 wherein the non-esterifying antifreeze is an ether-alcohol having at least one ether linkage between two carbon atoms, and having at least one secondary carbon atom bearing a hydroxyl group.

4. The composition of claim 1 wherein the non-esterifying antifreeze is an ester having at least one ester linkage between two carbon atoms.

5. The composition of claim 1 wherein the non-esterifying antifreeze has the structure R^1-O-CH_2-CH(OR^2)-R^3, wherein R^1 is C_{1-8}alkyl, and R^2 and R^3 are the same or different and independently selected from hydrogen or C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group.

6. The composition of claim 5 wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen, and R^3 is C_{1-8}alkyl moiety.

7. The composition of claim 5 wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen and R^3 is methyl.

8. The composition of claim 5 wherein R^1, R^2 and R^3 are C_{1-8}alkyl.

9. The composition of claim 1 wherein the non-esterifying antifreeze has the structure R^4-CH(OR^5)-CH_2-O-CH_2-CH(OR^2)-R^3, wherein R^2, R^3, R^4 and R^5 are the same or different and independently selected from hydrogen and C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group.

10. The composition of claim 9 wherein R^4 is C_{1-8}alkyl and R^5 is hydrogen.

11. The composition of claim 9 wherein R^4 is C_{1-8}alkyl and R^5 is C_{1-8}alkyl.

12. The composition of claim 5 or 9 wherein at least one oxygen atom is bound to -CO(C_{1-8}alkyl) to form an ester.

13. The composition of claim 1 wherein the non-esterifying antifreeze is propylene glycol monomethyl ether having the structure $CH_3OCH_2CH(OH)CH_3$.

14. The composition of claim 1 wherein the non-esterifying antifreeze is propylene glycol monoethyl ether having the structure $CH_3CH_2OCH_2CH(OH)CH_3$, propylene glycol monopropyl ether having the structure $CH_3CH_2CH_2OCH_2CH(OH)CH_3$, or propylene glycol monoisopropyl ether having the structure $CH_3CH(CH_3)OCH_2CH(OH)CH_3$.

15. The composition of claim 1 wherein the non-esterifying antifreeze is dipropylene glycol having the structure $CH_3CH(OH)CH_2OCH_2CH(OH)CH_3$.

16. The composition of claim 1 wherein the non-esterifying antifreeze is dipropylene glycol methyl ether having the structure $CH_3CH(OCH_3)CH_2OCH_2CH(OH)CH_3$, dipropylene glycol ethyl ether having the structure $CH_3CH(OCH_2CH_3)CH_2OCH_2CH(OH)CH_3$, or dipropylene glycol acetate having the structure $CH_3CH(OCOCH_3)CH_2OCH_2CH(OH)CH_3$.

17. The composition of claim 1 wherein the non-esterifying antifreeze is present at a concentration ranging from about 10% to about 75% by weight of the composition.

18. The composition of claim 1 wherein the non-esterifying antifreeze is present at a concentration ranging from 15% to 50% by weight of the composition.

19. The composition of claim 1 wherein the organic acid germicide is an alpha-hydroxy carboxylic acid having a pKa between about 2.8 and about 4.2.

20. The composition of claim 19 wherein the alpha-hydroxy carboxylic acid is glycolic acid, lactic acid, malic acid, mandelic acid, citric acid, tartaric acid, or mixtures thereof.

21. The composition of claim 1 wherein the organic acid germicide is formic acid, acetic acid, propionic acid, benzoic acid, caprylic acid, capric acid, hydroxybenzoic acid, or mixtures thereof.

22. The composition of claim 1 wherein the organic acid germicide is present at a concentration between about 0.25% and about 7.5% by weight of the composition.

23. The composition of claim 1 wherein the organic acid germicide is present at a concentration between 2% and 5% by weight of the composition.

24. The composition of claim 1 wherein the composition is formulated as a solution.

25. The composition of claim 1 wherein the composition is formulated as a cream or gel.

26. The composition of claim 1 further comprising a textural modifier, a surfactant, an odorant, a colorant, or mixtures thereof.

27. A method for disinfecting a substrate, comprising contacting the substrate with an effective amount of the freeze-resistant aqueous disinfecting composition of claim 1.

28. The method of claim 27 wherein the substrate is skin.

29. The method of claim 27 wherein the substrate is a teat of a dairy cow.

30. A two-part freeze-resistant disinfecting system comprising a first part and a second part adapted to be mixed to yield an aqueous disinfecting composition, wherein prior to mixing the first part comprises a metal chlorite and a chlorite-stable antifreeze, and the second part comprises (a) an organic acid germicide and a non-esterifying antifreeze, or (b) an inorganic acid and either an alcohol or a non-esterifying antifreeze, wherein each of the chlorite-stable and non-esterifying antifreezes contain from 4 to 16 carbon atoms and have no primary carbon atom bearing a hydroxyl group.

31. The system of claim 30 wherein the metal chlorite is an alkali or alkaline earth chlorite.

32. The system of claim 30 wherein the metal chlorite is sodium chlorite or potassium chlorite.

33. The system of claim 30 wherein the metal chlorite is sodium chlorite.

34. The system of claim 30 wherein the metal chlorite is present in the first part at a concentration such that, when combined with the second part, it is present within the

disinfecting composition at a concentration ranging from about 0.005% to about 1% by weight.

35. The system of claim 30 wherein the metal chlorite is present in the first part at a concentration such that, when combined with the second part, it is present within the disinfecting composition at a concentration ranging from 0.05% to 0.5% by weight.

36. The system of claim 30 wherein the metal chlorite is present in the first part at a concentration such that, when combined with the second part, it is present within the disinfecting composition at an concentration ranging from 0.1% to 0.4% by weight.

37. The system of claim 30 wherein the chlorite-stable antifreeze is an ether having at least one ether linkage between two carbon atoms.

38. The system of claim 30 wherein the chlorite-stable antifreeze is an ether-alcohol having at least one ether linkage between two carbon atoms, and having at least one secondary carbon atom bearing a hydroxyl group.

39. The system of claim 30 wherein the chlorite-stable antifreeze is an ester having at least one ester linkage between two carbon atoms.

40. The system of claim 30 wherein the chlorite-stable antifreeze has the structure R^1-O-CH_2-CH(OR^2)-R^3, wherein R^1 is C_{1-8}alkyl, and R^2 and R^3 are the same or different and independently selected from hydrogen or C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group.

41. The system of claim 40 wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen, and R^3 is C_{1-8}alkyl moiety.

42. The system of claim 40 wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen and R^3 is methyl.

43. The system of claim 40 wherein R^1, R^2 and R^3 are C_{1-8}alkyl.

44. The system of claim 30 wherein the chlorite-stable antifreeze has the structure R^4-CH(OR^5)-CH_2-O-CH_2-CH(OR^2)-R^3, wherein R^2, R^3, R^4 and R^5 are the same or different and independently selected from hydrogen and C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group.

45. The system of claim 44 wherein R^4 is C_{1-8}alkyl and R^5 is hydrogen.

46. The system of claim 44 wherein R^4 is C_{1-8}alkyl and R^5 is C_{1-8}alkyl.

47. The system of claim 40 or 44 wherein at least one oxygen atom is bound to -CO(C_{1-8}alkyl) to form an ester.

48. The system of claim 30 wherein the chlorite-stable antifreeze is propylene glycol monomethyl ether having the structure $CH_3OCH_2CH(OH)CH_3$.

49. The system of claim 30 wherein the chlorite-stable antifreeze is propylene glycol monoethyl ether having the structure $CH_3CH_2OCH_2CH(OH)CH_3$, propylene glycol monopropyl ether having the structure $CH_3CH_2CH_2OCH_2CH(OH)CH_3$, or propylene glycol monoisopropyl ether having the structure $CH_3CH(CH_3)OCH_2CH(OH)CH_3$.

50. The system of claim 30 wherein the chlorite-stable antifreeze is dipropylene glycol having the structure $CH_3CH(OH)CH_2OCH_2CH(OH)CH_3$.

51. The system of claim 30 wherein the chlorite-stable antifreeze is dipropylene glycol methyl ether having the structure $CH_3CH(OCH_3)CH_2OCH_2CH(OH)CH_3$,

dipropylene glycol ethyl ether having the structure $CH_3CH(OCH_2CH_3)CH_2OCH_2CH(OH)CH_3$, or dipropylene glycol acetate having the structure $CH_3CH(OCOCH_3)CH_2OCH_2CH(OH)CH_3$.

52. The system of claim 30 wherein the chlorite-stable antifreeze is present at a concentration ranging from about 10% to about 75% by weight of the first part.

53. The system of claim 30 wherein the chlorite-stable antifreeze is present at a concentration ranging from 15% to 50% by weight of the first part.

54. The system of claim 30 wherein the second part comprises the organic acid and the non-esterifying antifreeze.

55. The system of claim 54 wherein the organic acid and the non-esterifying antifreeze of the second part is the composition of any one of claims 1-23.

56. The system of claim 30 wherein the second part comprises the inorganic acid and either the alcohol or the non-esterifying antifreeze.

57. The system of claim 56 wherein the inorganic acid is selected from phosphoric acid, monosodium acid phosphate, sulfuric acid, hydrochloric acid, and sodium bisulfate.

58. The system of claim 56 wherein the inorganic acid is present in the second part at a concentration such that, when combined with the first part and before reacting therewith, it is present within the disinfecting composition at an initial concentration ranging from 0.001% to 2% by weight.

59. The system of claim 56 wherein the inorganic acid is present in the second part at a concentration such that, when combined with the first part and before

reacting therewith, it is present within the disinfecting composition at an initial concentration ranging from 0.01% to 1.0% by weight.

60. The system of claim 56 wherein the second part comprises the inorganic acid and the alcohol.

61. The system of claim 60 wherein the alcohol is a polyol.

62. The system of claim 61 wherein the polyol is glycerine, sorbitol or propylene glycol.

63. The system of claim 56 wherein the second part comprises the inorganic acid and the non-esterifying antifreeze.

64. The system of claim 63 wherein the non-esterifying antifreeze is an ether having at least one ether linkage between two carbon atoms.

65. The system of claim 63 wherein the non-esterifying antifreeze is an ether-alcohol having at least one ether linkage between two carbon atoms, and having at least one secondary carbon atom bearing a hydroxyl group.

66. The system of claim 63 wherein the non-esterifying antifreeze is an ester having at least one ester linkage between two carbon atoms.

67. The system of claim 63 wherein the non-esterifying antifreeze has the structure R^1-O-CH_2-CH(OR^2)-R^3, wherein R^1 is C_{1-8}alkyl, and R^2 and R^3 are the same or different and independently selected from hydrogen or C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group.

68. The system of claim 67 wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen, and R^3 is C_{1-8}alkyl moiety.

69. The system of claim 67 wherein R^1 is C_{1-8}alkyl moiety, R^2 is hydrogen and R^3 is methyl.

70. The system of claim 67 wherein R^1, R^2 and R^3 are C_{1-8}alkyl.

71. The system of claim 63 wherein the non-esterifying antifreeze has the structure R^4-CH(OR^5)-CH_2-O-CH_2-CH(OR^2)-R^3, wherein R^2, R^3, R^4 and R^5 are the same or different and independently selected from hydrogen and C_{1-8}alkyl, and each secondary carbon atom of the C_{1-8}alkyl moiety is optionally substituted with a hydroxyl group.

72. The system of claim 71 wherein R^4 is C_{1-8}alkyl and R^5 is hydrogen.

73. The system of claim 71 wherein R^4 is C_{1-8}alkyl and R^5 is C_{1-8}alkyl.

74. The system of claim 67 or 71 wherein at least one oxygen atom is bound to -CO(C_{1-8}alkyl) to form an ester.

75. The system of claim 63 wherein the non-esterifying antifreeze is propylene glycol monomethyl ether having the structure $CH_3OCH_2CH(OH)CH_3$.

76. The system of claim 63 wherein the non-esterifying antifreeze is propylene glycol monoethyl ether having the structure $CH_3CH_2OCH_2CH(OH)CH_3$, propylene glycol monopropyl ether having the structure $CH_3CH_2CH_2OCH_2CH(OH)CH_3$, or propylene glycol monoisopropyl ether having the structure $CH_3CH(CH_3)OCH_2CH(OH)CH_3$.

77. The system of claim 63 wherein the non-esterifying antifreeze is dipropylene glycol having the structure $CH_3CH(OH)CH_2OCH_2CH(OH)CH_3$.

78. The system of claim 63 wherein the non-esterifying antifreeze is dipropylene glycol methyl ether having the structure $CH_3CH(OCH_3)CH_2OCH_2CH(OH)CH_3$, dipropylene glycol ethyl ether having the structure $CH_3CH(OCH_2CH_3)CH_2OCH_2CH(OH)CH_3$, or dipropylene glycol acetate having the structure $CH_3CH(OCOCH_3)CH_2OCH_2CH(OH)CH_3$.

79. The system of claim 63 wherein the alcohol or non-esterifying antifreeze is present at a concentration ranging from about 10% to about 75% by weight of the second part.

80. The system of claim 63 wherein the alcohol or non-esterifying antifreeze is present at a concentration ranging from 15% to 50% by weight of the second part.

81. The system of claim 30 wherein the first part is formulated as a solution, cream or gel.

82. The system of claim 30 wherein the second part is formulated as a solution, cream or gel.

83. The system of claim 30 wherein the first part, second part, or both the first and second parts further comprises a textural modifier, a surfactant, an odorant, a colorant, or mixtures thereof.

84. A method for disinfecting a substrate, comprising contacting the substrate with an effective amount of the disinfecting composition of claim 30.

85. The method of claim 84 wherein the substrate is skin.

86. The method of claim 84 wherein the substrate is a teat of a dairy cow.

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(57) Abstract

A freeze-resistant topical germicide for application to skin, such as the teat of a dairy cow. The germicide may be a one-part composition or a two-part system. The one-part disinfecting composition comprises an organic acid germicide and a non-esterifying antifreeze. The two-part system comprises a first part and a second part adapted to be mixed to yield the disinfecting composition. The first part comprises a metal chlorite and a chlorite-stable antifreeze, and the second part comprises an organic acid germicide and a non-esterifying antifreeze, or an inorganic acid and either an alcohol or a non-esterifying antifreeze.

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 771 528 A (RICKETTS DAVID J.) 7 May 1997 (1997-05-07)	1,3,4,9, 10,15, 26-29
Y	column 1, line 1 - line 5 column 2, line 53 -column 3, line 22 claims 1,5,6	30-55, 81-86
X	WO 97 15649 A (RECKITT & COLMAN) 1 May 1997 (1997-05-01)	1-29
Y	page 1, line 12 -page 4, line 7 tables 1,2	30-86
Y	US 5 185 161 A (E.A.DAVIDSON) 9 February 1993 (1993-02-09) the whole document	30-55, 81-86

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 June 2000	10. 07. 2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fort, M

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/19987

C.(Continuation) DOCUMENTS C NSIDERED T BE RELEVANT

Category *	Citation of document, with indication,where appropnate, of the relevant passages	Relevant to claim No.
Y	WO 96 18300 A (ALCIDE CORPORATION) 20 June 1996 (1996-06-20) the whole document	30-86
Y	WO 97 09054 A (ALCIDE CORPORATION) 13 March 1997 (1997-03-13) the whole document	30-86
A	US 4 945 110 A (KYLE BROODEN ET AL.) 31 July 1990 (1990-07-31)	
A	DATABASE WPI Derwent Publications Ltd., London, GB; AN 1996-368102 XP002140432 NISSAN GOSEI KOGYO KK: "Liquid composition for preventing mamillitis of dairy cows-contains monoglyceride caprylate and/or monoglyceride(s) caprate and is applied in form of a spray or as dipping liq." cited in the application abstract & JP 08 175989 A 9 July 1996 (1996-07-09)	

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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/19987

Box I Observations where certain claims were f und unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-29, 30-53 (partially), 54-55, 81-86(partially)

A freeze resistant aqueous disinfecting composition comprising an organic acid germicide and a non-esterifying antifreeze and, optionally, a second part comprising a metal chlorite and a chlorite-stable antifreeze and a method for disinfecting a subtrate using the same

2. Claims: 30-53(partially), 56-80, 81-86(partially)

A two-part freeze-resistant disinfecting composition wherein the first part comprises an inorganic acid and either an alcohol or a non-esterifying antifreeze and the second part comprises a metal chlorite and a chlorite-stable antifreeze and a method for disinfecting a subtrate using the same.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/19987

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0771528 A	07-05-1997	CA 2156331 A	18-02-1997
		US 5534266 A	09-07-1996
		US 5720984 A	24-02-1998
WO 9715649 A	01-05-1997	GB 2306499 A	07-05-1997
		AU 718194 B	06-04-2000
		AU 7374196 A	15-05-1997
		BR 9611215 A	01-06-1999
		CN 1202925 A	23-12-1998
		EP 0904343 A	31-03-1999
		GB 2306500 A,B	07-05-1997
		NZ 320903 A	28-10-1999
US 5185161 A	09-02-1993	US 4986990 A	22-01-1991
		US RE36064 E	26-01-1999
		AT 84224 T	15-01-1993
		AU 584080 B	18-05-1989
		AU 4151785 A	11-10-1985
		BR 8506045 A	25-03-1986
		CA 1314477 A	16-03-1993
		DE 3586959 A	18-02-1993
		DE 3586959 T	29-04-1993
		DK 531885 A	18-11-1985
		EG 17596 A	30-06-1991
		EP 0176558 A	09-04-1986
		ES 541411 D	16-01-1987
		ES 8702793 A	01-04-1987
		FI 854497 A	14-11-1985
		GR 850689 A	22-07-1985
		HU 40335 A	28-12-1986
		IL 74684 A	15-08-1989
		IN 160430 A	11-07-1987
		JP 7045368 B	17-05-1995
		JP 61501495 T	24-07-1986
		MC 1721 A	15-12-1986
		MW 3785 A	14-09-1988
		MX 161768 A	20-12-1990
		NO 854623 A	19-11-1985
		NZ 211434 A	06-01-1989
		OA 8138 A	31-03-1987
		RO 95098 A	15-09-1988
		WO 8504107 A	26-09-1985
		US 5100652 A	31-03-1992
		ZA 8502033 A	26-02-1986
WO 9618300 A	20-06-1996	US 5651977 A	29-07-1997
		US 5597561 A	28-01-1997
		AT 182742 T	15-08-1999
		AU 4601296 A	03-07-1996
		DE 69511244 D	09-09-1999
		DE 69511244 T	02-03-2000
		EP 0744895 A	04-12-1996
		ES 2138764 T	16-01-2000
WO 9709054 A	13-03-1997	US 5772985 A	30-06-1998
US 4945110 A	31-07-1990	NONE	